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1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,079	ALVAREZ ET AL.	
	Examiner	Art Unit	
	Ronald T. Niebauer	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9-12 and 14-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9-12 and 14-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 November 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/29/07,10/11/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

After the first office action (1/24/07), applicants amended the claim set necessitating an election of species requirement (see 8/17/07).

Applicant's election of SEQ ID NO:1 (native chlorotoxin, compare page 10 line 18 of the specification) as the chlorotoxin derivative and temozolomide as the chemotherapeutic agent in the reply filed on 10/17/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The procedure for examination of Markush type claims is highlighted in MPEP section 803.02:

> Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable, the provisional election will be given effect and examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.
> The examination will be extended to the extent necessary to determine patentability of the Markush-type claim.

In the instant case, the elected species were found in the prior art and the claims were found to be unpatentable (via 35 USC 103) over the prior art. In the course of searching for the species, other prior art was uncovered that reads on other species and is cited herein.

In the reply filed 7/17/07 claims 7-8,13 were cancelled. In the reply filed 10/25/07 claims 18-21 were added. Claims 1-6,9-12,14-21 are under consideration. Any rejection and/or objection not specifically addressed is herein withdrawn.

Claim Objections

Claim 6,11 are objected to because of the following informalities: the claims recite the same agents (cisplatin, fluorouracil) within the same group more than once. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6,9-12,14-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained for claims 1-6,9-12,14-17 and necessitated by amendment for new claims 18-21.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial

variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to methods or compositions of chlorotoxin or chlorotoxin derivatives.

(1) Level of skill and knowledge in the art:

The level of skill in the art is high.

(2) Partial structure:

The claims (claims 1,9,14 and dependent claims) recite that the chlorotoxin derivative can comprise particular sequences, portions thereof, and combinations thereof. There are many

peptides within the genus. For example SEQ ID NO:13 (TTX1X2X3MX4X5K) which is 9 amino acids in length can have any amino acid at position X2 and X4 and numerous amino acids at X1,X3,X5. In considering the possible variability, there are over 4800 different 9 amino acid peptides possible. Further, there are many peptide portions and combinations of peptides. Hence, there is substantial variability in the genus.

The sequence listing includes 95 sequences (some of which may not be applicable to the current argument). Since the genus includes well over 4800 different sequences, the 95 sequences do not even represent two percent of the peptides within the genus.

Since there are a substantial variety of polypeptides possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

The claims recite that the chlorotoxin derivatives, portions thereof and combinations thereof are useful for treating cancer. However, no direction is provided as to what portions are necessary to be useful in treating cancer. As claimed, any portion or combination would meet the claim limitations. No direction is provided as to what portions or combinations are useful in treating cancer. The specification (page 10 lines 25-32) recites the phrase core binding sequences, however no common core is taught for all of the derivatives. One of skill in the art would not recognize which portions and combinations would be useful for treating cancer.

(5) Method of making the claimed invention:

Synthesis of peptides is described in example 11.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 1,9,14 and dependent claims is/are broad and generic, with respect to all possible derivatives encompassed by the claims. The possible structural variations are limitless to any derivative. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the polypeptides beyond those polypeptides specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of polypeptides identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of polypeptides embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Response to Amendment/Arguments – written description

Applicants argue (7/12/07) that the claims as amended overcome the rejection due to the limitations to the chlorotoxin derivative introduced into claims 1,9, and 14.

The arguments have been fully considered but they are not persuasive.

Although a limitation has been introduced into the claim, the claims remain broad. As discussed above, SEQ ID NO:13 alone represents over 4800 different peptides. Further, there are many peptide portions and combinations of peptides. Hence, there is substantial variability in the genus. Since there are a substantial variety of polypeptides possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

For these reasons and the reasons set forth previously, claims 1-6,9-12,14-21 fail to comply with the written description requirement.

Claim Rejections - 35 USC § 102 – maintained claims 14-17

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 14-17 remain rejected under 35 U.S.C. 102(b) as being anticipated by Soroceanu et al. (Cancer Research, November 1, 1998, Vol. 58, pages 4871-4879 as cited previously).

Soroceanu teach the administration of chlorotoxin (CTX), specifically ^{125}I radiolabeled CTX (abstract, page 4876) (compare claims 14,16,17 of the current invention) as a method of detection, for example, for detection of gliomas and glioblastomas (page 4871 1st two paragraphs), specifically human glioma cells in mice (page 4876) (compare claims 14,15 of the current invention).

Regarding claim language, section 2111.04 of the MPEP states:

> Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:
> (A) " adapted to " or "adapted for " clauses;
> (B) " wherein " clauses; and
> (C) " whereby " clauses.
> ..... a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'"

In the instant case, the recitation 'for detecting the presence of cancer' (claim 14) does not require an additional step to be performed, claim 14 requires an administration step. The recitation 'wherein the cancer is...' (claim 15) does not limit the patient population since a method of detection can be for a diseased or non-diseased patient population. In the instant case, Soroceanu teach the administration of ^{125}I radiolabeled CTX to mice, specifically mice with implanted human glioma cells (page 4876), which meets the current limitations.

It is noted that SEQ ID NO:1 of the current invention is native chlorotoxin. Thus Soroceanu meets the claim limitations since chlorotoxin comprises SEQ ID NO:1, the elected chlorotoxin derivative of the current invention.

Claims 14-17 remain rejected under 35 U.S.C. 102(e) as being anticipated by Lyons et al. (US 6,667,156 as cited previously).

Lyons teach the administration of radiolabeled ^{125}I to a patient for detection of glioblasotmas (claims 1,2,3,4,5,6 and example 8) (compare claims 14-17 of the current invention).

Regarding claim language, section 2111.04 of the MPEP states:

> Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:
> (A) " adapted to " or "adapted for " clauses;
> (B) " wherein " clauses; and
> (C) " whereby " clauses.
> ..... a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'"

In the instant case, the recitation 'for detecting the presence of cancer ' (claim 14) does not require an additional step to be performed, claim 14 requires an administration step. The recitation 'wherein the cancer is...' (claim 15) does not limit the patient population since a method of detection can be for a diseased or non-diseased patient population. In the instant case, Lyons teach the administration of ^{125}I radiolabeled CTX to patients (claim 1) which meets the current limitations.

It is noted that SEQ ID NO:1 of the current invention is native chlorotoxin. Thus, Lyons meets the claim limitations since chlorotoxin comprises SEQ ID NO:1, the elected chlorotoxin derivative of the current invention.

Response to Amendment/Arguments – 102 claims 14-17

Applicants argue (7/12/07) that the claims as amended read on 'labeled chlorotoxin' derivative. Applicants argue that the rejection is moot

The arguments have been fully considered but they are not persuasive.

Applicants have elected SEQ ID NO:1 (i.e. chlorotoxin) as the species of chlorotoxin derivative. Claim 14 reads on a chlorotoxin comprising SEQ ID NO:1. It is unclear why applicant regards the previous rejection as moot since the claim still reads on native chlorotoxin (SEQ ID NO:1, the elected species). In fact, in the response to the restriction requirement (10/17/07) applicant has stated: 'Thus, Applicant respectfully elects SEQ ID NO:1 as the species of chlorotoxin derivative. Claims 1-6,9-12, and 14-17 read on the elected species, SEQ ID NO:1'. As discussed above, Soroceanu teach SEQ ID NO:1 (chlorotoxin) (abstract, page 4876), hence the structural limitations are met. As discussed above, Lyons teach SEQ ID NO:1 (chlorotoxin) (claim 1), hence the structural limitations are met. Both of the prior art references teach radiolabelled chlorotoxin meeting the claimed limitations.

For these reasons and the reasons set forth previously, the 102 rejection of claims 14-17 is maintained.

Claim Rejections - 35 USC § 102 – new rejection

Claims 1,4-6,9-12,18-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Samoylova et al. (US 2003/0216322) as evidenced by Merck Manual (on-line version www.merck.com/mmhe 'methotrexate' entry).

Samoylova teach peptides for recognition and targeting of glial cell tumors (title). Samoylova teach compositions comprising a peptide and a chemotherapeutic agent (claim 4, section 0068) (compare claim 9 of the current invention). Samoylova teach peptides such as ELRGDSLP (claim 6), which comprises a portion (RG, amino acids 25 and 26 of chlorotoxin SEQ ID NO:1 of the current invention) of chlorotoxin thus meeting the structural limitations of a portion of a chlorotoxin derivative as recited in claims 1,9 and dependent claims. Samoylova teach chemotherapeutic agents such as methotrexate (section 0066) (compare claim 11,6 of the current invention). The Merck Manual teaches (page 2) that methotrexate is an anti-metabolite (a universal fact so priority date not relevant - see MPEP 2124) (compare claim 10,5 of the current invention).

Samoylova teach a need for therapies for brain tumor patients (seciton 0008) and specifically teach patient populations with glioblastomas (section 0004). Samoylova teach the administration of a peptide conjugated to a chemotherapeutic agent (methotrexate) in example 3 specifically section 0132 (compare claim 4,18,20 of the current invention) and further experiments in human patients (example 4 section 0135). In addition to simultaneous administration via a conjugate, Samoulova teach compositions in which the peptide and chemotherapeutic agent are not conjugated to one another (section 0068). Samoylova teach compositions with a pharmaceutically acceptable carrier (section 0069) (compare claim 19 of the current invention).

Regarding claim language, section 2111.04 of the MPEP states:

> Claim scope is not limited by claim language that suggests or makes optional but does not require steps to be performed, or by claim language that does not limit a claim to a particular structure. However, examples of claim language, although not exhaustive, that may raise a question as to the limiting effect of the language in a claim are:
> (A) " adapted to " or "adapted for " clauses;

> (B) " wherein " clauses; and
> (C) " whereby " clauses.
> ..... a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'"

In the instant case, the recitation 'for treating cancer' (claim 9) does not limit the claim to a particular structure. The recitation 'wherein the cancer is ...' (claim 12) does not limit the claim to a particular structure.

Claim Rejections - 35 USC § 103 – new rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6,9-12,18-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Samoylova et al. (US 2003/0216322) and Stupp et al. (The Lancet v2 Sept 2001 552-560).

As discussed above, Samoylova teach peptides for recognition and targeting of glial cell tumors (title). Samoylova teach compositions comprising a peptide and a chemotherapeutic agent (claim 4, section 0068) (compare claim 9 of the current invention). Samoylova teach a need for therapies for brain tumor patients (seciton 0008) and specifically teach patient populations with glioblastomas (section 0004). Samoylova teach the administration of a peptide conjugated to a chemotherapeutic agent (methotrexate) in example 3 specifically section 0132 (compare claim 4,18,20 of the current invention) and further experiments in human patients (example 4 section 0135). In addition to simultaneous administration via a conjugate, Samoulova teach compositions in which the peptide and chemotherapeutic agent are not conjugated to one another (section 0068). Samoylova teach compositions with a pharmaceutically acceptable carrier (section 0069) (compare claim 19 of the current invention).

Samoylova et al. does not expressly recite an embodiment with chlorotoxin as the peptide (instead Samoylova teach phage derived peptides). Samoylova does not expressly teach the chemotherapeutic agent temozolomide.

Samoylova does teach chlorotoxin (section 0010) (equivalent to SEQ ID NO:1 of the current invention, the elected species of chlorotoxin) as a peptide that specifically binds to glioma cells. Since Samoylova also teach that the peptides of the invention are cell-binding peptides (section 0034) one would be motivated to substitute the chlorotoxin peptide for the phage derived peptides particularly since Samoylova specifically teach glioma as a target and

also since chlorotoxin is taught to have high-affinity specific binding to glioma cells (section 0010).

Stupp teach the administration of the alkylating agent/chemotherapeutic agent temozolomide (abstract) (compare claims 5,6,10,11 of the current invention). Stupp specifically teach temozolomide for brain tumours and glioma (abstract). Stupp teach temozolomide with other active agents against brain tumours (abstract and page 557-558). Stupp specifically teach that temozolimide can be used sequentially with other agents (page 557 1st column last paragraph) and also in a variety of combination dosing schedules (page 557-558) (compare claims 2-3 of the current invention), and in combination with more than one agent (page 558 first column last paragraph) (compare claim 21 of the current invention).

One would have been motivated to combine the chemotherapeutic agent temozolomide as taught by Stupp into the method/compositions of Samoylova since both references deal with therapeutics specifically of brain tumors. Both references motivate the use of combination therapies. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Further, it is noted that it is obvious to combine known elements to be used for the same purpose and that the motivation to combine them flows logically from their being taught in the prior art (MPEP 2144.06). In the instant case, both chlorotoxin and temozolomide were each individually taught in methods and compositions for treating brain tumors.

It has been recently held that "Neither §103's enactment nor *Graham*'s analysis disturbed

the Court's earlier instructions concerning the need for caution in granting a patent based on the combination of elements found in the prior art." KSR v. Teleflex, 550 U.S. ___, 82 USPQ2d 1385, 1389 (2007). The KSR court stated that "a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." KSR at 1389. The Supreme Court stated that there are "[t]here cases decided after Graham [that] illustrate this doctrine." KSR at 1395. "In United States v. Adams, 383 U.S. 39, 40, 148 USPQ 479 (1966) . . .[t]he Court recognized that when a patent claims a structure already known in the prior art that is altered by the mere substitution of one element for another known in the field, the combination must do more than yield a predictable result." KSR at 1395. Thus, the mere substitution of one known element for another to obtain a predictable result is obvious.

Furthermore, The KSR court concluded that "obvious to try" may be an appropriate test under 103. The Supreme Court stated in *KSR*

> When there is motivation
>
> > "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

In the instant case, Samoylova teach phage derived peptides. Since the peptides are taught as cell-binding peptides (section 0034) and chlorotoxin is a specific cell binding peptide, one would have substituted the known elements (chlorotoxin for the phage derived peptides) and would have yielded predictable results to one of ordinary skill in the art at the time of the invention. In the instant case, all the claimed elements were taught in the prior art (Samoylova – chlorotoxin; Stupp – temozolomide) and one skilled in the art could have combined the elements

as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Response to Amendment/Arguments – 103 rejections

Although this is a new rejection, the arguments to the previous 103 rejection will be addressed to extent that they apply to the new rejection.

Applicants argue that the prior art teaches covalent linkages between the components of the composition and as such would be conjugates. Applicants argue that the conjugates do not teach or suggest the current invention.

The arguments have been fully considered but they are not persuasive.

It is noted that the claims currently read on a composition (claim 9 for example) comprising a chlorotoxin derivative and a chemotherapeutic agent. The claim language is open to the chlorotoxin and chemotherapeutic agent being conjugates. There is nothing in the claim language to exclude conjugates. Further, the newly cited art clearly teach embodiments in which the peptide and chemotherapeutic agent are not conjugated to one another (section 0068 of Samoylova).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 9-12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1,13 of copending Application No. 10/522,810 ('810) in view of Stupp et al. (The Lancet v2 Sept 2001 552-560).

'810 teach a subunit of chlorotoxin (i.e. a portion of chlorotoxin - compare claim 9 of the current invention) in a composition conjugated to a cytotoxic agent for binding to cancer cells (claim 13).

'810 does not teach the specific cytotoxic agent of the current invention.

Stupp specifically teach temozolomide compositions for brain tumours and glioma (abstract). Stupp teach temozolomide with other active agents against brain tumours (abstract and page 557-558). Stupp teach that temozolomide is a cytotoxic agent (page 553 2nd full paragraph line 13). As discussed above it would have been obvious to substitute the agent of Stupp into other compositions such as that of '810 that target cancer cells.

This is a provisional obviousness-type double patenting rejection.

Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1,23 of copending Application No. 11/731,661 ('661).

'661 teach a method of administering a chlorotoxin conjugate (claim 1) and a chemotherapeutic agent (claim 23) to a patient with tumors which reads on claim 1 of the current invention.

This is a provisional obviousness-type double patenting rejection.

Claims 1-6,9-12,18-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims1,23 of copending Application No. 11/731,661 ('661) in view of Samoylova et al. (US 2003/0216322) and Stupp et al. (The Lancet v2 Sept 2001 552-560).

'661 teach a method of administering a chlorotoxin conjugate (claim 1) and a chemotherapeutic agent (claim 23).

As discussed above, Samoylova and Stupp teach the remaining claim limitations. In the instant case, all the claimed elements were taught in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

This is a provisional obviousness-type double patenting rejection.

Claims 1,4,9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4,21 of copending Application No. 11/547,875 ('875) in view of Stupp et al. (The Lancet v2 Sept 2001 552-560).

'875 teach administration of a composition comprising chlorotoxin (claim 4) and a cytotoxic agent (claim 21) to patients with cancer.

'875 does not teach the specific cytotoxic agent of the current invention.

Stupp specifically teach temozolomide compositions for brain tumours and glioma (abstract). Stupp teach temozolomide with other active agents against brain tumours (abstract and page 557-558). Stupp teach that temozolomide is a cytotoxic agent (page 553 2nd full paragraph line 13). As discussed above it would have been obvious to substitute the agent of Stupp into other compositions such as that of '875.

This is a provisional obviousness-type double patenting rejection.

Claims 1-6,9-12,18-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4,21 of copending Application No. 11/547,875 ('875) in view of Stupp et al. (The Lancet v2 Sept 2001 552-560) and Samoylova et al. (US 2003/0216322).

'875 teach administration of a composition comprising chlorotoxin (claim 4) and a cytotoxic agent (claim 21) to patients with cancer.

As discussed above, Samoylova and Stupp teach the remaining claim limitations. In the instant case, all the claimed elements were taught in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective

functions and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

The examiner has identified three copending Applications which have been rejected under Double Patenting above. Because of Applicant's prolific Patent and Application portfolio, the burden is shifted to Applicant to identify all relevant Applications and Patents and to include said Applications and Patents on any terminal disclaimer filed.

The claims as specified above are directed to an invention not patentably distinct from the claims specified above of commonly assigned 10/522,810; 11/731,661; 11/547,875. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned 10/522,810; 11/731,661; 11/547,875, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly

assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ronald T. Niebauer whose telephone number is 571-270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rtn

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ANISH GUPTA
PRIMARY EXAMINER